EXHIBIT 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	PAOLETTI
U.S. Serial No.	:	08/228,926
Filing Date	:	April 18, 1994
Title of the Invention	:	MODIFIED VACCINIA VIRUS AND METHODS FOR MAKING AND USING THE SAME
Confirmation No.	:	4171
Examiner	:	Mary Mosher
Art Unit	:	1648

745 Fifth Avenue
New York, NY 10151

FILED VIA EFS

DECLARATION OF DR. ENZO PAOLETTI

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

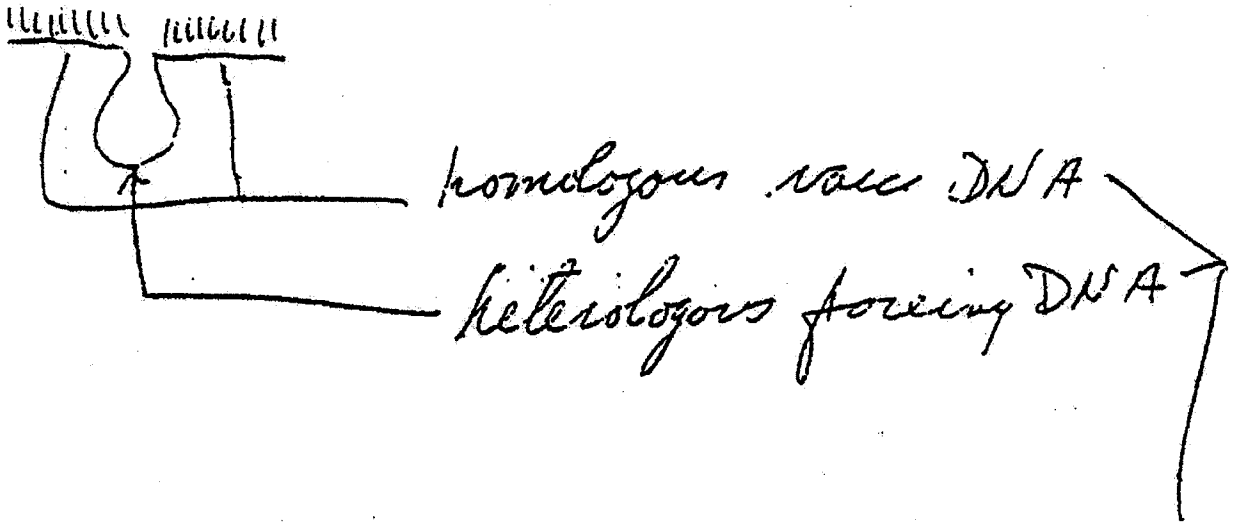
Dear Sir:

ENZO PAOLETTI declares and states that:

1. I am a named inventor on the above-captioned application ("the present application"). I am familiar with the claims of the present application as pending.

2. I submit herein a true copy of my handwritten notes from a date prior to the December 24, 1981 filing date of priority U.S. application Serial No. 06/334,456, which matured into U.S. Patent No. 4,769,330. The handwritten notes were authored solely by me in the United States. The handwriting in the handwritten notes is solely my handwriting.

3. The handwritten notes evince my sole conception of the invention as claimed. Note especially the following in the attached:



4. In the above illustration, the handwriting is: "homologous vacc[inia] DNA" and "heterologous forei[gn] DNA".

5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful, false statements may jeopardize the validity of the application or any patent issuing thereon.

NOV. 15, 2008
Date

DR. ENZO PAOLETTI

EP has original

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August 27, 1980. It's a great beautiful day in New Hampshire. The sky is blue & the weather warm. These past few days have been really nice vacationing up here at Lee's. I hope the Volvo repairs won't cost too much. I called the lab & received some of the most data that ever been involved in an experiment. The marker rescue experiments that Eileen began in late June have finally been scored and they are positive. It is possible to rescue segments of mitotic DNA with infectious vaccinia virus. The L and S variants have really proven to be very valuable in showing marker rescue. The donor DNA sequences are unique so there is no background as would be found with TS reversion & deletions. In addition, being able to cleave the donor DNA within or without the unique sequence allow for unequivocable data to be gathered. The ability to

Exhibit 1

demonstrate marker rescue will really be a boom to the molecular genetics of the poxviruses, but there are potential applications of this basic technique that are just boggling to consider at this time, for example, we will now be able to manipulate the vaccinia genome by DNA recombinant techniques such that one can now begin to seriously consider doing experiments such as:

A) the construction of viable deletion mutants, i.e. identifying & deleting the vaccinia genome of unnecessary DNA sequences and

B) the insertion of "foreign DNA" into the vaccinia genome either at the deletion site that exists in the genome or the newer deletions that will be generated as per A above or by inserting foreign DNA at a number of restriction sites that are available and/or may be tailored for particular purposes. What we have

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generated is a potential new cloning vector for foreign DNA by the technique of in vivo DNA recombination as demonstrated by marker rescue. This new cloning vector, vaccinia virus, is unique consideration because it is so large in terms of DNA size, it is cytoplasmic in replication and has little danger of oncogenic considerations. The virus has been used successfully in the eradication program leading to the eradication of smallpox. One of the most interesting purposes for using this newfound process is the construction of vaccines to various pathogenic organisms by insertion of the genetic information sequences (into the vaccinia genome) that are responsible for the synthesis of neutralizing antigen(s). Thus, as an example it will be possible to insert into the vaccinia genome the DNA sequences from Herpes simplex virus that

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are responsible for neutralizing titers
initially. These antigens would
then be expressed after natural
infection and would result in
a vaccination against herpesvirus.
The possibility of eliminating herpes 1
and herpes 2 with is a serious
problem and also implicated in
cervical carcinoma is quite
exciting. This is only an example
and although the first approximation
to this new technology is admittedly
a simplistic one, there is no
reason to consider that it can not be
done. Its actuality appears to be only
a function of learning or applying
appropriate existing technologies or
the modification or extension of
various DNA recombinant
technologies to this particular
problem. With sophistication
that comes with learning the
system it will be possible
to string a number of these
foreign DNA sequences together

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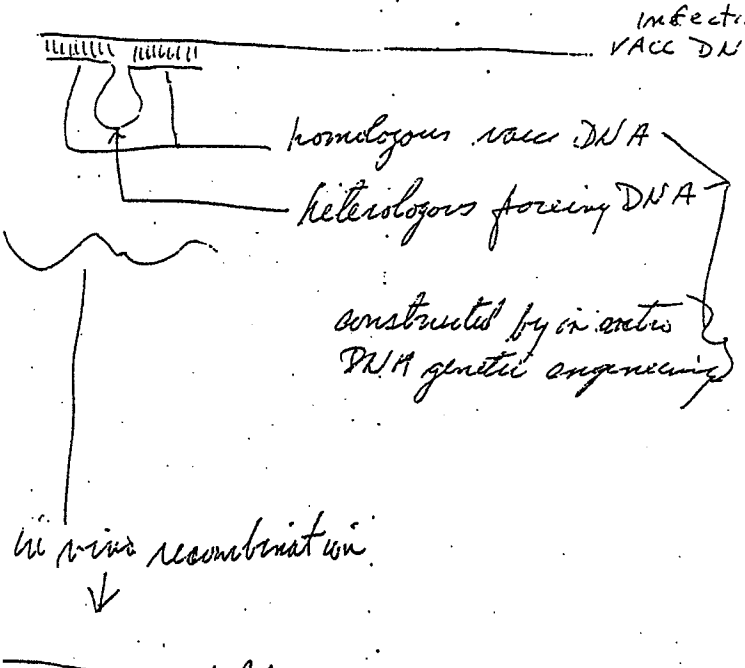
like a rosary such that one vaccinia virus appropriately manipulated can give rise to a number of vectors by a number of different pathogens like a multivalent vaccination.



infectious vaccinia virus containing a genome w a foreign DNA insert

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There are a number of interesting questions of course that needs to be answered but their answers can undoubtedly be found in manipulation of the system. For example - when in the vaccinia genome will a foreign DNA be expressed early/late - next to a strong/weak vaccinia promoter - tandem repeats of foreign DNA inserts for amplification

The laboratory phase of the work will be very exciting and the potential applications of this discovery are overwhelming given this vantage point